

WHO publishes global priority list of antibiotic-resistant bacteria to guide research

The World Health Organization has developed a global priority list of antibiotic-resistant bacteria to identify the most important resistant bacteria globally and to help prioritize research and development of new antibiotics (www.who.int/medicines/publications/WHO-PPL-Short_Summary_25Feb-ET_NM_WHO.pdf?ua=1).

The report categorizes bacteria into 'critical', 'high' and 'medium' priority groups. Bacteria in need of urgent treatment solutions include *Pseudomonas aeruginosa*, *Acinetobacter baumannii* and *Enterobacteriaceae* which are resistant to multiple antibiotics and responsible for severe infections.

The report was chaired by Professor Evelina Tacconelli, executive committee member of the European Society of Clinical Microbiology and Infectious Diseases in collaboration with the World Health Organization.

Professor Tacconelli said: 'This report marks a major step forward in identifying which bacteria pose the greatest risk for patient care... We hope that it will drive governments and research groups working in antibiotic development to set the right research priorities that will reduce the burden of antibiotic-resistant infections globally.'

Epilepsy classification updated

In the first update in almost three decades, the International League Against Epilepsy has published a new classification system for epilepsy (<https://doi.org/10.1111/epi.13670>). This includes many types of seizures not captured in the older version, allowing clinicians and patients to make more informed decisions concerning treatment.

The new classification includes the whole clinical picture of epilepsy, which may point to potential causes and groupings of different types of seizures that could lead to further advances in research and treatment.

Increased bone resorption in premenopausal South Asian women may cause higher risk of osteoporosis

Researchers have examined bone resorption and effects of vitamin D in over 370 pre- and postmenopausal South Asian and white Caucasian women in the UK (Darling et al, 2017) who participated in the longitudinal D-FINES (Diet, Food Intake, Nutrition and Exposure to the Sun in Southern England) cohort study (2006–7).

Researchers measured levels of urinary N terminal telopeptide over a 12-month period to

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assess how much bone was being broken down. Premenopausal South Asian women had higher urinary levels of this byproduct than their white Caucasian counterparts, indicating higher levels of bone resorption than expected for their age. Typically high levels of urinary N terminal telopeptide are only found in postmenopausal women, as was the case in this study.

Lead author, Dr Andrea Darling from the University of Surrey, said: 'We have found that premenopausal South Asian women have the same level of bone resorption as a woman who has been through the menopause. We need to investigate further whether these women simply have higher levels of both bone resorption and bone formation or if there is something more worrying occurring in their skeletal system, in terms of higher than expected bone resorption, increasing their susceptibility to bone diseases and fractures.'

Individuals with a larger seasonal change in vitamin D concentration showed increased bone resorption, suggesting it may be as important clinically to ensure a stable and steady vitamin D concentration, as well as one high enough to be optimal for bone health.

Darling AL, Hart KH, Gossiel F et al (2017) Higher bone resorption excretion in South Asian women vs. White Caucasians and increased bone loss with higher seasonal cycling of vitamin D: Results from the D-FINES cohort study. *Bone* 98: 47–53. <https://doi.org/10.1016/j.bone.2017.03.002>

Preoperative psychological ill-health linked to increased risk of wound complications post-surgery

Poor healing of wounds and increased pressures on the NHS through readmissions are more likely if surgery is carried out on people with anxiety or depression (<https://doi.org/10.1002/bjs.10474>).

Researchers studied the relationship between three measures of anxiety and/or depression and seven adverse surgical outcomes using data collected before and after hip replacements, knee replacements, hernia repairs and varicose vein operations. The sample included 176 827 patients admitted for surgery between 2009 and 2011 in England.

The team found a strong correlation between preoperative psychological problems and readmissions for wounds failing to

heal properly and for urinary and bleeding complications. The odds of experiencing wound complications after a hip replacement were 1.17 times greater for patients with moderate anxiety or depression than those without. Similar results were seen across all types of operations and were larger for patients with extreme anxiety or depression.

Lead researcher, Philip Britteon, from The University of Manchester's Centre for Health Economics, said: 'Psychological health can often be overlooked in preoperative assessment. Addressing anxiety or depression in advance of surgery has the potential to help people recover more quickly and save the NHS time and money in the longer term.'

International criteria for electrocardiographic screening and interpretation in athletes

New internationally recognized electrocardiogram criteria (Drenzer et al, 2017) cast fresh light on the current debate relating to the accuracy and cost-efficiency of the electrocardiogram as a screening tool to identify athletes with potential life-threatening heart conditions. They also show promise for the future of a screening programme for all young people across the UK, whether elite athletes, grass-roots players or the general population, as the rate of false positives has fallen from 21.8% to 4.3% as well as the cost of accurate heart screening being reduced by at least 20%.

Sudden cardiac death is the leading cause of mortality in young athletes during sport. These new criteria are likely to lead to significant reductions in the number of 'false positives' from electrocardiogram testing, confirming that this simple test is the most efficient way of identifying young athletes with undiagnosed cardiac conditions.

Professor Sanjay Sharma, Consultant Cardiologist and Professor of Inherited Cardiac Disease and Sports Cardiology at St George's, University of London, commented: 'The publication of these recommendations



Professor Sanjay Sharma, Consultant Cardiologist and Professor of Inherited Cardiac Disease and Sports Cardiology, St George's, University of London

represents the culmination of two decades of research and numerous scientific meetings working towards the development of a clear guide to the proper evaluation of electrocardiogram abnormalities in athletes.

Professor Sharma added: 'For the first time ever, our studies also now represent an international consensus – which could potentially be rolled out to all young people involved in grass-roots sports, not just those playing at a professional level and with access to expert cardiologists via their clubs and training academies.'

Every week, 12 apparently fit and healthy young (aged 35 years and under) people in the UK die from a previously undiagnosed heart condition. In 80% of cases, there will have been no signs or symptoms. In Italy, where screening is mandatory for all young people engaged in organized sport, the incidence of young sudden cardiac death has been reduced by 89%.

Drenzer JA, Sharma S, Baggish A et al (2017) International criteria for electrocardiographic interpretation in athletes. *Br J Sports Med* pii: bjsports-2016-097331. <https://doi.org/10.1136/bjsports-2016-097331>

Multi-parametric MRI and transrectal ultrasound-guided biopsy in prostate cancer: diagnostic accuracy

Using multi-parametric magnetic resonance imaging (MRI) might allow men with high levels of serum prostate-specific antigen to avoid unnecessary prostate biopsy and improve diagnostic accuracy.

The PROMIS trial enrolled 740 men, 576 of whom underwent multi-parametric MRI followed by transrectal ultrasound-guided biopsy and template prostate mapping biopsy (Ahmed et al, 2017). On template prostate mapping biopsy, 408 men (71%) had cancer, with 230 (40%) cases clinically significant. For clinically significant cancer, multi-parametric MRI was more sensitive but less specific than transrectal ultrasound-guided biopsy. Of 740

patients 44 (5.9%) reported serious adverse events, including eight cases of sepsis.

Using multi-parametric MRI as triage might allow 27% of patients to avoid a primary biopsy and diagnosis of 5% fewer clinically insignificant cancers. Multi-parametric MRI could reduce unnecessary biopsies and over-diagnosis of clinically insignificant prostate cancer and improve detection of clinically significant cancer.

Ahmed HU, El-Shater Bosaily A, Brown LC et al; PROMIS study group (2017) Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study. *Lancet* **389**(10071): 815–822. [https://doi.org/10.1016/S0140-6736\(16\)32401-1](https://doi.org/10.1016/S0140-6736(16)32401-1)

Podoplanin causes thrombosis in patients with malignant brain tumours

Podoplanin expression by primary brain tumours induces platelet aggregation and is associated with hypercoagulability and a high risk of venous thromboembolism. This increased risk of venous thromboembolism is independent of age, sex and tumour type (<https://doi.org/10.1182/blood-2016-06-720714>).

Lung disease costs the UK £11 billion each year

Estimating the Economic Burden of Respiratory Illness in the UK, a report by the British Lung Foundation (www.blf.org.uk/what-we-do/our-research/economic-burden), breaks down the cost of respiratory health by lung condition. With costs of £9.9 billion falling directly on the NHS and £1.2 billion on the wider economy through missing work, respiratory health is taking a huge financial toll on the UK.

Biologic treatments for inflammatory bowel disease help heal the intestine

A systematic review and meta-analysis (<https://doi.org/10.1111/apt.14030>) has shown that anti-tumour necrosis factor and anti-integrin biological agents induce mucosal healing in patients with ulcerative colitis, with adalimumab inferior to infliximab or combination therapy. Infliximab and adalimumab were similar in patients with Crohn's disease.

European Society for Blood and Marrow Transplantation, Marseille, 26–29 March

Letermovir: a ‘game changer’ for cytomegalovirus infection after allogeneic haematopoietic stem cell transplant

Primary prophylaxis with letermovir significantly reduces the risk of clinically significant cytomegalovirus infections and decreases all-cause mortality at 24 weeks after allogeneic haematopoietic stem cell transplant, according to a large randomized, placebo-controlled, phase 3 study (Ljungman et al, 2017). Letermovir was also well tolerated, with no increase in bone marrow or renal toxicity.

Lead investigator Professor Per Ljungman, Department of Medicine, Karolinska Institutet, Stockholm, Sweden, commented: ‘This is a game changer. We have for many years known that being cytomegalovirus seropositive is negative for survival post-haematopoietic stem cell transplant. It has also been shown that having cytomegalovirus infection is negative for outcome, and this study puts the last stone in the wall. Assuming regulatory approval, we now have a means to improve outcome, because we have an effective drug that was quite non-toxic in this phase 3 study.’

The study included 570 adult cytomegalovirus seropositive allogeneic haematopoietic stem cell transplant recipients with undetectable plasma cytomegalovirus DNA within 5 days of randomization. Letermovir 480 mg/

day (240 mg/day in patients receiving ciclosporin) or placebo was initiated by 28 days post-haematopoietic stem cell transplant and continued for up to 14 weeks. Patients who discontinued the study early for any reason or who had missing data at week 24 post-transplant were considered study failures.

On the primary endpoint, 37.5% of the letermovir group developed clinically significant cytomegalovirus infection by week 24 post-haematopoietic stem cell transplant or were considered study failures compared to 60.6% of the placebo group ($P < 0.0001$). Reduced rates of clinically significant cytomegalovirus infection were seen in letermovir-treated patients at high and low risk of cytomegalovirus.

At week 24, all-cause mortality was 10.2% for letermovir-treated patients *vs* 15.1% for the placebo group. At week 24 in 21.5% of the letermovir group had cytomegalovirus viraemia *vs* 41.8% of the



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placebo group. The adverse events more commonly reported in the letermovir group than the placebo group were vomiting, peripheral oedema, atrial arrhythmias and serum alanine aminotransferase levels $>5x$ the upper limit of normal.

Letermovir is an investigational, once-daily antiviral under development for the prevention of cytomegalovirus infection. It is a non-nucleoside cytomegalovirus inhibitor (3,4 dihydroquinazoline)

and inhibits viral replication by specifically targeting the viral terminase complex. Letermovir has been granted orphan designation in Europe, the USA and Japan for prevention of cytomegalovirus infection and disease in at-risk populations.

Ljungman P, Marty FM, Chemaly R et al (2017) Letermovir (LET) for prevention of cytomegalovirus (CMV) infection: results from a phase iii randomized, double-blind, placebo (PBO)-controlled trial in adult allogeneic hematopoietic cell transplant (alloHCT) recipients. Presented during the Presidential Session. 43rd Annual Meeting of the European Society for Blood and Marrow Transplantation, Marseille, France: 26–29 March

EBMT reports record number of haematopoietic stem cell transplants

In 2015, there were 42 171 haematopoietic stem cell transplants in 37 626 patients (43% allogeneic) in Europe and affiliated countries. This is a record, according to the latest European Society for Blood and Marrow Transplantation (EBMT) activity survey report, covering 655 centres in 48 countries (Passweg et al, 2017).

The use of haploidentical donors for allogeneic haematopoietic stem cell transplants reached 2012 in 2015 – a 291% increase since 2005. Both bone marrow

and peripheral blood are being used as the stem cell source for haploidentical haematopoietic stem cell transplants, with a greater increase reported for the latter.

The main indications for haematopoietic stem cell transplants are lymphoid malignancies (67%; 20% allogeneic), myeloid malignancies (25%; 96% allogeneic), non-malignant disorders (6%; 90% allogeneic) and solid tumours (4%; 3% allogeneic). Use of allogeneic haematopoietic stem cell transplants in patients with chronic lymphocytic

leukaemia has fallen from 504 patients in 2011 to 255 in 2015. The EBMT considers that this is most likely the result of the development of potentially very effective drug treatments for chronic lymphocytic leukaemia.

Passweg JR, Baldomero H, Bader P et al for the European Society for Blood and Marrow Transplantation (2017) Use of haploidentical stem cell transplantation continues to increase, the 2015 European Society for Blood and Marrow Transplant activity survey report. Abstract A210. 43rd Annual Meeting of the European Society for Blood and Marrow Transplantation, Marseille, France: 26–29 March

Mite-proof bedcovers may reduce asthma flare-ups in children

Bedcovers that form a barrier to house dust mites appear to reduce asthma flare-ups in children, according to a study of 284 children with asthma who tested positive for mite allergy, one of the most common asthma triggers (Murray et al, 2017).

The children, aged 3–17 years, enrolled in the study after suffering an asthma flare-up or exacerbation that required treatment in the emergency department or as an inpatient at one of 14 hospitals in north-west England. After encasing their mattresses, duvets and pillows with mite-proof covers or placebo covers, the children were followed for a year. Neither the children, nor the investigators nor their health-care professionals knew which set of covers the children received.

Compared to those in the placebo arm of the trial, children sleeping with the mite-proof covers were less likely to have a severe asthma exacerbation that resulted in an emergency department visit or hospital admission (29.3% vs 41.5%), had a 45% reduced risk of having



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an asthma exacerbation that resulted in an emergency department visit or hospitalization and the requirement for systemic corticosteroids.

The treatment group also saw a significantly longer time between using the mite-proof covers and the first exacerbation that resulted in an emergency room visit or hospitalization with the need for systemic corticosteroids.

The authors estimated the cost of the bedcovers to be about £130. Dr Clare S Murray, clinical senior lecturer at the University of Manchester and the Royal Manchester Children's Hospital, and lead author, commented: 'This simple measure may reduce asthmatic exacerbations that lead to emergency department visits or hospitalization, particularly in younger children who are allergic only to dust mites'.

Murray CS, Foden P, Sumner H, Shepley E, Custovic A, Simpson A (2017) Preventing severe asthma exacerbations in children: a randomised trial of mite impermeable bedcovers. *Am J Respir Crit Care Med* <https://doi.org/10.1164/rccm.201609-1966OC>

Microwave helmet yields fast and safe evaluation of chronic subdural haematoma

Microwave measurements can be used for rapid detection of intracranial bleeding in patients with traumatic brain injuries, shows a small new study (Ljungqvist et al, 2017).

The study compared 20 patients hospitalized for surgery of chronic subdural haematoma with 20 healthy volunteers. The patients were examined with microwave measurements which were compared to traditional computed tomography scans. The results show that microwave measurements have great potential to detect intracranial bleeding in this group of patients.

'The result is very promising even though the study is small and only focused on one

type of head injury. The microwave helmet could improve the medical assessment of traumatic head injuries even before the patient arrives at the hospital', commented lead author Dr Johan Ljungqvist, specialist in neurosurgery at the Sahlgrenska University Hospital, Gothenburg, Sweden. He added: 'The result indicates that the microwave measurements could be useful in ambulances and in other care settings.'

Ljungqvist J, Candefjord S, Persson M, Jönsson L, Skoglund T, Elam M (2017) Clinical evaluation of a microwave-based device for detection of traumatic intracranial hemorrhage. *J Neurotrauma* <https://doi.org/10.1089/neu.2016.4869>

Mediterranean diet adherence and risk of postmenopausal breast cancer

Researchers from the Netherlands investigated the relationship between adherence to the Mediterranean diet and risk of postmenopausal breast cancer (<https://doi.org/10.1002/ijc.30654>). In the Netherlands Cohort Study, 62 573 women aged 55–69 years provided information on dietary and lifestyle habits in 1986, and were followed up for cancer incidence until 2007.

The findings support an inverse association between Mediterranean diet adherence and, particularly, receptor-negative breast cancer, even in a non-Mediterranean population. This may have important implications for prevention because receptor-negative breast cancer has a poorer prognosis.

Antidepressants and anti-anxiety drugs linked to increased risk of hip fracture

Older individuals who had fallen and broken a hip used antidepressant and anti-anxiety medications more frequently than the general older population, found a Norwegian study (<https://doi.org/10.1111/bcp.13244>).

The analysis measured drug levels in individuals' blood samples, which provided a more precise measure than asking participants if they took the medications or examining their medical records. Indeed, drugs were often present in these samples despite no information in patients' medical records.

'We were surprised to find that so many patients had centrally-acting drugs in their blood without doctors being aware of this use. Several of the detected drugs increase the risk of falling, which underscores the clinical relevance of these findings,' said Dr Ragnhild Waade, lead author from the Center for Psychopharmacology, Diakonhjemmet Hospital, Oslo, Norway.